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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/278,601	07/21/1994	DAVID KNIPE	DFCI363A	6837
21874	7590	09/22/2004	EXAMINER	
EDWARDS & ANGELL, LLP			MOSHER, MARY	
P.O. BOX 55874				
BOSTON, MA 02205			ART UNIT	PAPER NUMBER
			1648	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	08/278,601	KNIPE ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Mary E. Mosher, Ph.D.	1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 02 July 2004.

2a) This action is **FINAL**.                    2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 12-21, 31, 36, 41, 50-63, 65, 67-69, 71-73 and 75-104 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) 18-21, 31, 41, 68, 69, 71-73 and 75-97 is/are allowed.

6) Claim(s) 12-15, 17, 50-63, 98-100, 102 and 103 is/are rejected.

7) Claim(s) 16, 65, 67, 101 and 104 is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_

4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_

5) Notice of Informal Patent Application (PTO-152)

6) Other: \_\_\_\_\_

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### **DETAILED ACTION**

Claims 12-21, 31, 36, 41, 50-63, 65, 67-69, 71-73, 75-104 are pending.

Claims 12-15 remain rejected under 35 U.S.C. 102(g) or, in the alternative, under 35 U.S.C. 103(a), as being drawn to the same invention as the lost count, or on the grounds of estoppel. The claims have been amended to restore the language regarding the ability of the virus to effect an antibody subclass shift, but still retain the broad scope of "a method of eliciting an immune response." The Board, in paper no. 107, page 49, pointed out a distinction between "recitation of inherent features of a composition" which does not render the composition patentable, and "methods of using a composition based upon its unknown specific property, i.e. the ability to effect an antibody subclass shift." The Board also indicated acceptance of the argument that "such use would not have been obvious from the use of a mutant herpesvirus as a herpes vaccine." However, claims 12-15 have now been broadened so that they encompass the use of the mutant ICP8 or ICP27 herpesvirus as a herpes vaccine, even though the claims a nonobvious inherent property in the virus used in the method. Since the Board has ruled that applicants are not entitled to claim a method of using ICP8 or ICP27 as a herpesvirus vaccine, the amendment does not overcome the rejection over the lost count.

Claim 16 is objected to under 37 CFR 1.75 as being a duplicate of claim 18.

When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after

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allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 12-15 and 17 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating herpetic stromal keratitis or encephalitis, does not reasonably provide enablement for a method of treating an unspecified condition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. In the previous Office action, these claims were included in a rejection limiting enablement to treating herpes stromal keratitis using a herpesvirus which elicits the subclass shift or induces IFN-gamma. The claims have been amended to address the “subclass shift” claim element, but not the “treating” claim element. On reconsideration, the specification is seen as disclosing treatment of herpetic encephalitis as well as herpetic keratitis, see specification page 15. However, as discussed in interference paper 107, pages 52-59, the court has refused to find broad generic claims enabled by specifications that demonstrate the enablement of only one or a few embodiments and do not demonstrate with reasonable specificity how to make and use other potential embodiments across the full scope of the claim. Since there is limited disclosure of conditions suitable for treatment with the viruses, enablement is seen as limited to treatment of the two disclosed conditions.

Claims 50-63, 98-100, 102, 103 are rejected under 35 U.S.C. 102(g) or, in the alternative, under 35 U.S.C. 103(a), as being drawn to the same invention as the lost count, or on the grounds of estoppel. Applicant argues that the claims are directed to

compositions including a herpesvirus having two or more deletions rendering the herpesvirus incapable of replication, and that this subject matter would not have been obvious in view of the interference count. It is noted that the claims recite "two or more mutations", not two or more deletions. However, the argument is not convincing because count 2 of the interference included "claim 49 of Knipe," which at the time was directed to a composition comprising HSV-1 or HSV-2 having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective "wherein the mutation is in the gene or genes encoding the proteins ICP8 or ICP27." It is maintained that "two or more genes" is obvious over "one or more genes".

Claim 36 remains rejected under 35 U.S.C. 102(b) as being anticipated by Dobson et al (Neuron 5:353-60, 1990). Applicant argues that Dobson teaches the "early intermediate gene ICP4, which inhibits replication," and that an "early intermediate gene" which "inhibits" replication is not a teaching of an early gene rendering the virus replication defective. It is noted that ICP4 is an immediate early gene, and that "early gene" can be variously interpreted to include or exclude immediate early genes. However, since applicant's claims consistently use the term "early gene" to refer to the immediate early gene ICP27, the term "early" is seen as including ICP4 as well. Furthermore, the ICP4 mutation does render the virus defective in replicating the genome, see the statement near the top of page 353, column 2 in Dobson, that mutants "replicate only in ICP4-expressing cells." Still further, Katz et al (Journal of Virology

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64:4288-4295, 1990) is cited as evidence that an ICP4 deletion mutant is at least as replication defective as an ICP27 mutant, see page 4291, second column.

***Allowable Subject Matter***

Please note, before this application can be allowed the examiner must consult with the administrative judge in charge of the interference regarding lost counts and estoppel; although every effort has been made to deal with these issues, the consultation with the judge has not yet occurred. Therefore, the following indication of allowable subject matter is tentative, pending consultation with the judge when all the claims appear allowable to the examiner.

The following is a statement of reasons for the indication of allowable subject matter:

Claims 65, 67, 101, 104 because the lost count does not specify the combination of deletion and nonsense mutations.

Claims 31, 41, 68, 69, 71, 72, 73, 75-97, because the interference did not include heterologous constructs, and because the disclosure and claims of e.g. Inglis patent 6541009 do not particularly point to mutations in ICP8, ICP27, or other genes essential for genome replication as appropriate for in vivo immunization vectors, with reasonable expectation of success. In addition, the rejection of claim 41 over Dobson is withdrawn in view of the amendment to the claim.

Claims 18-21, because treatment of herpetic stromal keratitis is enabled and distinct from the interference count.

Claims 18-21, 31, 41, 68, 69, 71-73, 75-97 are allowed.

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Claims 65, 67, 101, 104 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is 571-272-0906. The examiner can normally be reached on M-T and alternate F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

9/20/04

*Mary E. Mosher*  
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